

Quest Diagnostics Incorporated

33608 Ortega Highway
San Juan Capistrano, CA 92675

**Fax Cover Sheet****DATE:** June 7, 2000**TIME:** 1:25 PM Pacific Time**TO:** Quan
COMPANY:**PHONE:**
FAX: (949) 450-1764**FROM:** Cheryl Gallagher- Legal and
Compliance Department
Secretary to Steve Weiss**PHONE:** 949.728.4199**FAX:** 949.728.4957**E-MAIL:** gallaghc@questdiagnostics.com**RE:****COPY:****FAX:****Number of pages including cover sheet:** 6

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Re 08/482,402

To: Steven Weiss

949-728-4957

Courtesy Copy of Advisory Action
which will be mailed this week
5 pages including cover

Susan Ungar

703-305-2181

08/182,402

SERIAL NUMBER	FIGURE DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED:

Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☒ TIME PERIOD FOR RESPONSE:

- a) ☐ Is extended to run _____ or continues to run _____ from the date of the final rejection
- b) ☒ Expires three months from the date of the final rejection or from the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire less than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.135(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally submitted statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due in accordance with 37 CFR 1.182(a).

☒ Applicant's response to the final rejection, filed March 12, 1990 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☒ The proposed amendments to the claim and/or specification will not be entered and the final rejection stands because:

- a. ☐ There is no convincing showing under 37 CFR 1.148(b) why the proposed amendment is necessary and presented.
- b. ☒ They raise new issues that would require further consideration and/or search. (See Note).
- c. ☒ They raise the issue of new matter. (See Note).
- d. ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying appeal.
- e. ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: The limitation of "is immunogenic to human thyroid tissue metastasizing" in claim 38 raises the issue of immutability. It is unclear how the DNA construct can be immunogenic to human thyroid tissue. The DNA construct is the specification for the newly added (2.1.1) the non-allowable claims.

clear how the DNA construct can be immunogenic to human thyroid tissue. The DNA construct is the specification for the newly added (2.1.1) the non-allowable claims.

2. ☒ Upon the filing an appeal, the proposed amendment ☐ will be entered ☒ will not be entered and the status of the be as follows:

Claims allowed: None
Claims objected to: None
Claims rejected: 11-15

However:

☐ Applicant's response has overcome the following rejection(s):

4. ☐ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because _____

See attached

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficient reasons why it was not earlier presented

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☐ Other

SUSAN J. GUN
Primary Patent Examiner

The limitation of "immunogenic to human thyroid metastasizing" in claim 38 raises the issue of immutability. It is unclear how the DNA construct can be immunogenic to human thyroid tissue. The DNA construct is the specification for the newly added (2.1.1) the non-allowable claims.

I'm not clear how the DNA construct can be immunogenic to autoantibodies. The does not appear to be supp in the spec for the new claim.

Art Unit: 1642

1. Applicant's Amendment After Final filed March 12, 2000 will not be entered for the reasons disclosed on PTO Form 303.

2. If the amendment were to be entered the rejection drawn to claims 11-15 under 35 USC 103 would be maintained for the reasons previously disclosed in

Paper No. 12, Section 16, pages 9-11, Paper No. 17, Section 10, pages 5-6) and

Paper No. 20, Section 12, pages 5-6, Paper No. 25, Section 9, pages 3-6.

Applicant argues that (a) the references do not specifically teach nor suggest that a recombinant DNA encoding a secretable human thyroid peroxidase can be successfully produced, (b) Applicant submits a reference demonstrating that failure to produce a secretable ectodomain of a thyrotropin receptor and failure of the synthesized protein to recognize human autoantibodies to the full length protein.

The argument has been considered but has not been found persuasive because (a) the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Koller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Given the teachings of the prior art references, one of ordinary skill in the art would have expected to successfully produce a secretable human thyroid peroxidase (b) as drawn to the failure of the ectodomain to recognize human autoantibodies to the full length protein, Applicant is arguing limitations not recited in the claims as presently constituted. As drawn to the failure

Just an exam

claim 38 (new)

Art Unit: 1642

to produce a secretable ectodomain of a transmembrane protein, a review of the submitted reference reveals that the reference is drawn to a thyrotropin receptor which is a transmembrane protein. The reference specifically teaches the differences between thyroid peroxidase (TPO) and the thyrotropin receptor (TSHR) and specifically teaches that it is much more difficult to produce large quantities of conformationally intact TSHR than conformationally intact TPO (para bridging pages 2525) and specifically teaches that TSHR is an unstable protein and that this has made purification from the source impractical and that given these difficulties, a logical alternative approach is to attempt TSHR-ECD expression as a secreted protein (p. 2525, para 2). The reference further teaches that lack of success in producing the holoreceptor is attributed to its large, relatively hydrophilic seven-membrane-spanning regions and that the TSHR-ECD expressed in CHO cells is "largely nonsecreted" (col 2, p. 2531) and teach that the inescapable conclusion is that it is the protein that is producing the present difficulty (p. 2532, col 1). It is clear that the reference teaches that there are significant differences between TSHR and TPO in both stability and structure and that TSHR is not only an unstable protein but also has seven-membrane spanning regions as compared to the hydrophilic carboxylic membrane anchor of TPO. It is clear that the reference specifically states that it is the protein itself that is producing the difficulty. Further, even with the "difficulty", the reference specifically teaches that although TSHR-ECD is largely nonsecreted, the TSHR-ECD is (emphasis added) secreted. It does not appear that the membrane spanning region of TSHR is in any way related to the membrane anchor of TPO or of the gD protein or of the G protein described in

that's
the point -
not all
protein
are the
same

Serial No: 08/482,402

Page 4

Art Unit: 1642

Paper No. 12 and it does not appear that the difficulties encountered by Rapaport et al could be extrapolated to the teachings previously disclosed.

Country copy

[Signature]
Primary SUSAN UNGAR
PATENT EXAMINER

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DATE: June 7, 2000

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OUR FAX # 949-450-1764

OUR TELEPHONE # 949-450-1750

TO: Susan Ungar, Ph.D.

FAX: 703-308-4426

FROM: Quan L. Nguyen

RE: 08/482,402

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Dear Susan,

Attached is the Associate Power of Attorney for the above application. Thank you.

Yours,



Quan L. Nguyen

P.S. Please note the change in correspondence to Mr. Donald E. Stout. Thank you.

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